Impact of Intrathecal Cell Therapy with Autologous Stromal Cells on Short-Term Memory Binding in Early Alzheimer's Disease: One-Year Follow-up Assessment

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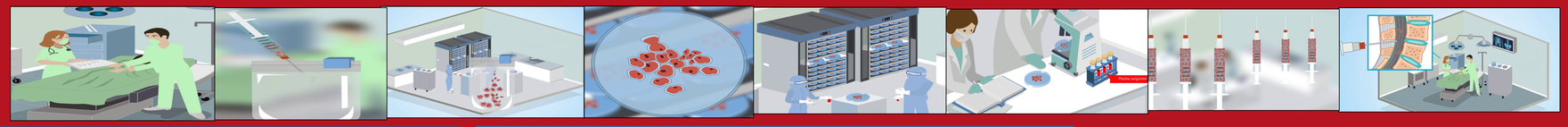
We had previously reported that the administration of bone marrow mesenchymal stromal cells (MSCs) therapy to two patients with mild AD dementia, led to a global increase in cerebral glucose metabolism, which was accompanied by significant improvement of visual short-term memory binding (VSTMB), a function known to be a marker of AD (Fernández-Guinea et al., 2019). We suggested that intrathecal administration of MSCs could be considered a new therapeutic strategy for AD dementia (Vaquero et al., 2019). We were interested in investigating the post-intervention durability of such cognitive improvements.

Method

Clinical procedures and experimental task:

2 patients received every three months 100 million of autologous MSCs by intrathecal route, until a total dose of 300 million. None received any other medication for its disease at the time of receiving cell therapy.



Participants:

N=6 Diagnosis of Alzheimer's disease. 2 of them received cellular therapy.

Without medication

Detection of beta-amyloid neuritic plaques (18F-Flutemetamol-PET).

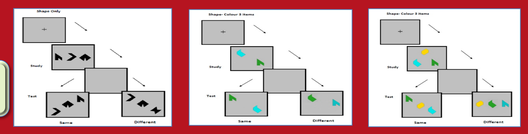
Brain glucose metabolism studied with 18F-FDG-PET

Neuropsychological assessment:

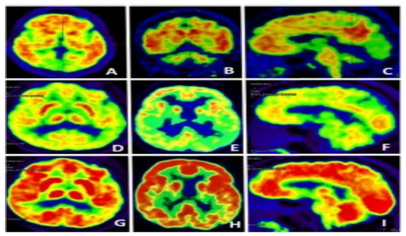
MMSE
Addenbrooke's Cognitive Examination
Barthel ADL Scale
Lawton and Brody IADL
Clinical Dementia Rating Scale
Rey Complex Figure Test
Rey Complex Figure Test
Stroop Test
TAVEC (Spanish CVLT)
WAIS-IV

VSTMB Test: **It requires subjects to detect whether or not two combinations of shape and colour change across two sequential arrays.**

This task has been proposed as a preclinical marker of AD (Dubois et al 2016).



Results

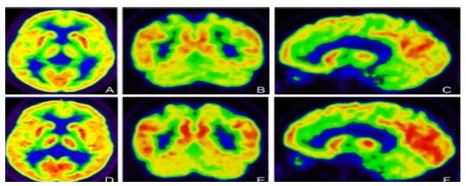


Case 1. A-C: beta-amyloid neuritic plaques with 18F-Flutemetamol-PET.

D-E: 18F-FDG-PET previous to cell therapy and one week after first intrathecal administration of 100 millions MSCs (G-I).

STMB TASK	PRE	POST 1	POST 2	POST 3 (END)	POST 4 (+1YR)
Shape Only	100%	100%	94%	100%	100%
Shape-Colour Binding	50%	62%	66%	62%	67%

Changes in 18F-FDG-PET in case 1 and case 2 from Vaquero et al, 2019.



Case 2. 18F-FDG-PET showing metabolic activity previous to cell therapy (A-C) and at the end of treatment (D-F).

STMB TASK	PRE	POST 1	POST 2	POST 3 (END)	POST 4 (+1YR)
Shape Only	88%	91%	88%	88%	91%
Shape-Colour Binding	52%	69%	66%	81%	44%

Single case statistics revealed that benefits drawn by treated patients from the therapy remained a year after. Using a more taxing version of the VSTMB test (memory load of 3 items) we observed that, after the therapy, the chance that an untreated AD patient would show more impairment was 75.45% (p= 0.24) for Case 1 and 89.23% (p=0.11) for case 2. This chance remained after 1 year post-treatment for Case 1 (75.45%, p=0.24) and increased for Case 2 (96.89%, p=0.031).

Conclusions

Intrathecal cell therapy with autologous MSCs increases cerebral glucose metabolism, being associated with neuropsychological improvements in patients experiencing early stages of AD. Improvements of memory functions known to be marker for AD in patients who underwent stem cell therapy remained stable after one year post-intervention. This type of cell therapy is safe, allowing distribution of donor cells in the whole brain. Administration of autologous MSCs should be considered as a new therapeutic strategy for Alzheimer's dementia and deserves further studies.

Fernández-Guinea, S., Zurita, M, Mucientes, J., García, E., Parra, M.A., Vaquero, J. (2019). Preliminary evidence of impact of intrathecal cell therapy with autologous stromal cells on short-term memory binding in early Alzheimer's disease cases. Alzheimer's and Dementia 15 (7): P929

Fernández-Guinea S, Zurita M, García-Zamora E, Mucientes J, López C, Fernández-Mateos C and Vaquero J (2019) Late Intrathecal Cell Therapy Increases Brain Glucose Metabolism and Improves the Long-Term Established Sequelae of Cerebral Hemorrhage. Int J Stem Cell Res Ther, 5 (2)

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Vaquero J, Zurita M, Bonilla C, Fernandez C, Rubio JJ,Mucientes J, et al. Progressive increase in brain glucose metabolism after intrathecal administration of autologous mesenchymal stromal cells in patients with diffuse axonal injury. Cytotherapy 2017;19:88–94.

Vaquero J, Zurita M, Mucientes J, Pascual MJ, Férnándiez-mateos C, García E, Férnández-Guinea S (2019) Intrathecal cell therapy with autologous stromal cells increases cerebral glucose metabolism and can offer a new approach to the treament of Alzheimer's type dementia. Cytotherapy, 21 (4):428-432.